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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	4

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/079,136	Applicant(s) STEWART ET AL.	
	Examiner Rodney P. Swartz, Ph.D.	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24July2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *9-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' Response to Restriction Requirement, received 24July2003, paper#9, is acknowledged.

Applicants elect, with traverse, Invention I, claims 1-8, 19, 20, drawn to composition of whole bacteria with modified protein production, classified in class 435, subclass 69.1. The traversal is on the grounds that the inventions are closely releated and that the search of both groups should not be burdensome. This is not found persuasive because of the reasons put forth in the original Restriction, i.e., each invention has acquired a separate status in the art as shown by their different classification, and because while the searches may overlap, the searches are not coextensive. The requirement is still deemed proper and is therefore made FINAL. Applicants elect under the Election of Species, *M. tuberculosis*, and Hsp70.

Claims 1-20 are pending. Claims 9-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

2. Claims 1-8, 19, and 20 drawn to *M. tuberculosis* and Hsp70 are under consideration.

Drawings

3. M.P.E.P. §2422.02, third paragraph, recites that "the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings." Figure 12 does not comply. Appropriate correction is required.

Specification

4. The disclosure is objected to because of the following informalities:

Page 4) line 12, 'Avium' should be 'avium',

Page 8) line 33, 'overexpressesing' should be 'overexpressing',

Page 10) line 12, '*BCG* should not be italicized,

Page 12) line 15, 'analysed' should be 'analyzed'; line 24, 'M. tuberculosis' should be italicized.

Page 13) line 1, 'centralised' should be 'centralized'; line 34, 'hybridised' should be 'hybridized',

Page 14) line 8, 'hybridised' should be 'hybridized',

Page 21) line 8, 'recognises' should be 'recognizes',

Page 27) line 14, insert 'for' between 'treatment' and 'AIDS'; what is significance of numbers '1' '2' and '3' between lines 15 and 16; what is significance of 'kb' in margin in line 17; line 29, '*Characterisation*' should be '*Characterization*',

Page 28) line 13, 'visualised' should be 'visualized',

Page 29) line 13, 'visualised' should be 'visualized'; lines 22 and 31, 'analysed' should be 'analyzed'; line 25, 'lyophilised' should be 'lyophilized',

Page 30) line 35, 'permeabilising' should be 'permeabilizing',

Page 31) line 19, '*Characterisation*' should be '*Characterization*',

Page 33) line 11, 'synthesised' should be 'synthesized',

Page 37) line 19, 'hybridisation' should be 'hybridization',

Page 38) line 36, what is the significance of [Wilson M, 2001 #38],

Page 39) line 1, 'prehybridisation' should be 'prehybridization'; lines 6 and 9, 'hybridisation' should be 'hybridization'; line 12, 'hybridised' should be 'hybridized'; lines 13 and 18, 'analysed' should be 'analyzed',

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, because claim 2 recites the limitation "modified protein expression" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 2 depends from claim 1 which recites modified protein "production". Claim 3 depends from claim 2, but does not correct the deficiency.

8. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, because the claims recite the limitation "wherein the heat shock protein comprises Hsp 60 or Hsp 70" in lines 1-2. There is insufficient antecedent basis for this limitation in the claims because claim 6 depends from claim 5 which depends from claim 1 which does not recite "heat shock protein". Likewise, claim 7 depends from claim 5 which depends from claim 1 which does not recite "heat shock protein".

9. Claims 19 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites "An immunogenic composition comprising an improved BCG vaccine wherein the vaccine comprises modified *M. bovis* having increased heat shock protein production." It is unclear whether the "modified" mycobacterium is a modified *M. bovis* BCG or another strain of *M. bovis*.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 4, 5, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Snewin et al (*Infection and Immunity*, 67(9):4586-4593, September 1999).

The instant claims are drawn to an immunogenic composition comprising mycobacteria wherein said mycobacteria comprises modified protein production and wherein the mycobacteria is *M. tuberculosis* and also wherein said composition further comprises a pharmaceutically acceptable carrier.

The instant claims do not restrict modified protein production to any particular type of modification.

Snewin et al teach a mycobacterial construct which is recombinant *M. tuberculosis* carrying a luciferase reporter enzyme from the American firefly (*Photinus pyralis*) (Abstract; section **Bacterial strains and growth conditions**, page 4587; section **Plasmid construction**, page 4587). This recombinant construct thus produces a protein not normally associated with the mycobacteria and therefore fulfills the criteria of "modified protein production" in the claim. Snewin et al also teach a murine infection model which utilizes the recombinant *M. tuberculosis* injected with a pharmaceutically acceptable carrier, i.e., saline (section **Murine infection model**, page 4587-4588).

12. Claims 1, 4, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayward et al (*Vaccine*, 17:1272-1281, 1999).

The instant claims are drawn to an immunogenic composition comprising mycobacteria wherein said mycobacteria comprises modified protein production and wherein the mycobacteria is *M. bovis* and also wherein said composition further comprises a pharmaceutically acceptable carrier.

The instant claims do not restrict modified protein production to any particular type of modification.

Hayward et al teach a mycobacterial construct which is a recombinant *M. bovis* BCG carrying an *E. coli* heat labile enterotoxin B-subunit (Abstract; **Materials and methods**, page 1273-1276). This recombinant construct thus produces a protein not normally associated with the mycobacteria and therefore fulfills the criteria of "modified protein production" in the claim. Hayward et al also teach a murine infection model which utilizes the recombinant mycobacteria injected with a pharmaceutically acceptable carrier, i.e., phosphate buffered saline (sections 2.6 to 2.8, page 1275).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 2, 3, 6, 7, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al (*Proc. Natl. Acad. Sci., USA*, 85:4267-4270, June 1988) in view of Hayward et al (*Vaccine*, 17:1272-1281, 1999).

The instant claims are drawn to an immunogenic composition comprising: 1) mycobacteria wherein said mycobacteria comprises modified protein production of heat shock

protein, and wherein the mycobacteria is *M. bovis* or *M.* tuberculosis and 2) wherein said composition further comprises a pharmaceutically acceptable carrier.

Young et al teach that stress proteins are important immune targets in mycobacterial disease, i.e., leprosy and tuberculosis, and that said stress proteins may have "immunoprophylactic" potential for a broad spectrum of human pathogens. (Title; Abstract; section **Materials and Methods**; section **Results and Discussion**). However, Young et al do not teach recombinant mycobacteria comprising said stress proteins for administration to subjects as immunogenic compositions

Hayward et al do teach a mycobacterial construct which is a recombinant *M. bovis* BCG carrying an *E. coli* heat labile enterotoxin B-subunit (Abstract; **Materials and methods**, page 1273-1276). Hayward et al also teach a murine infection model which utilizes the recombinant mycobacteria injected with a pharmaceutically acceptable carrier, i.e., phosphate buffered saline (sections 2.6 to 2.8, page 1275). In addition, Hayward et al suggest that such a recombinant *M. bovis* BCG may be suitable for other antigens (page 1280, first column, lines 9-35; page 1280, column 2, lines 13-27).

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the teachings and recombinant mycobacteria of Hayward et al to immunize subjects with mycobacteria which expresses the heat shock proteins taught by Young et al in order to produce an improved mycobacterial vaccine.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., whose telephone number is (703) 308-4244.

The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (703)308-3909. The facsimile telephone number for the Art Unit Group is (703) 872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-2035.

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

September 24, 2003